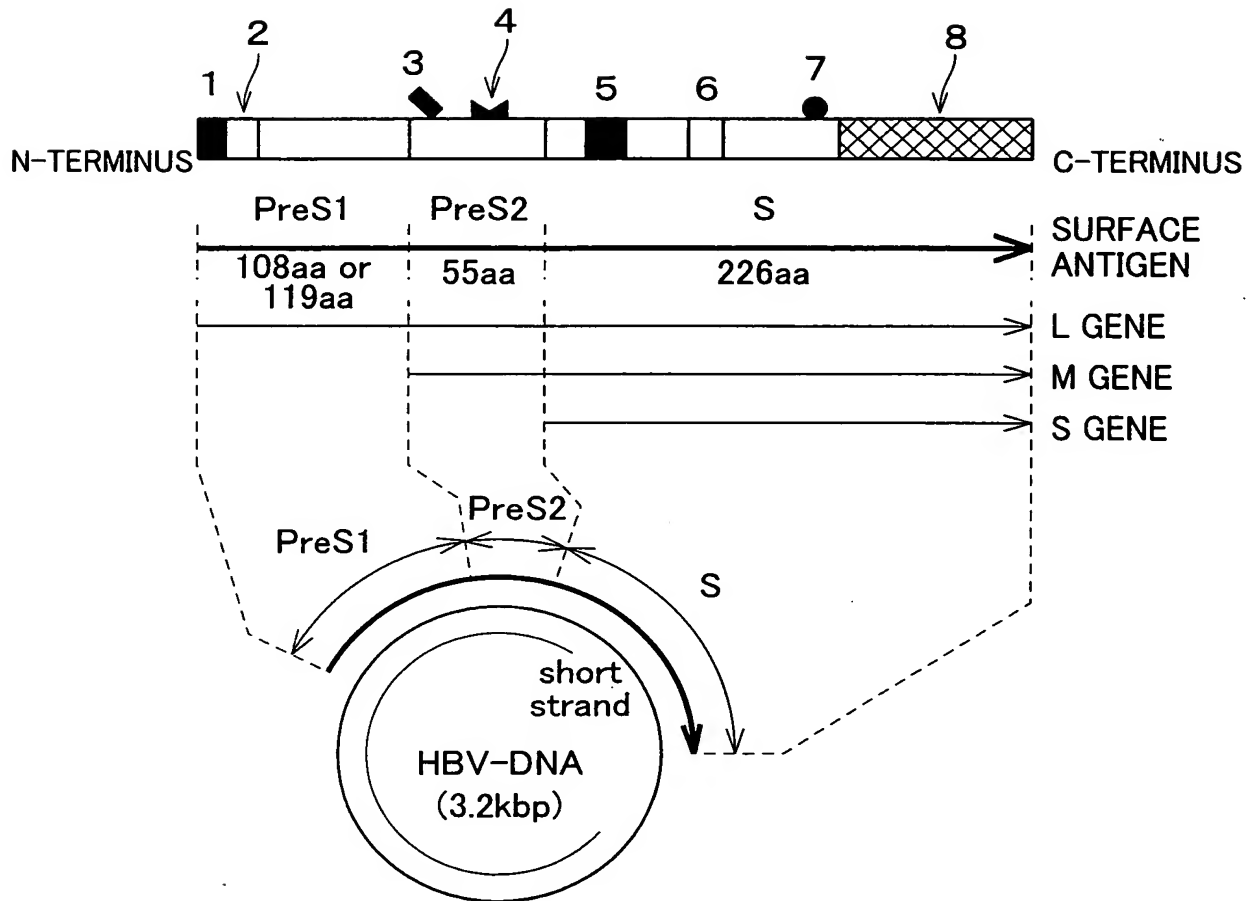


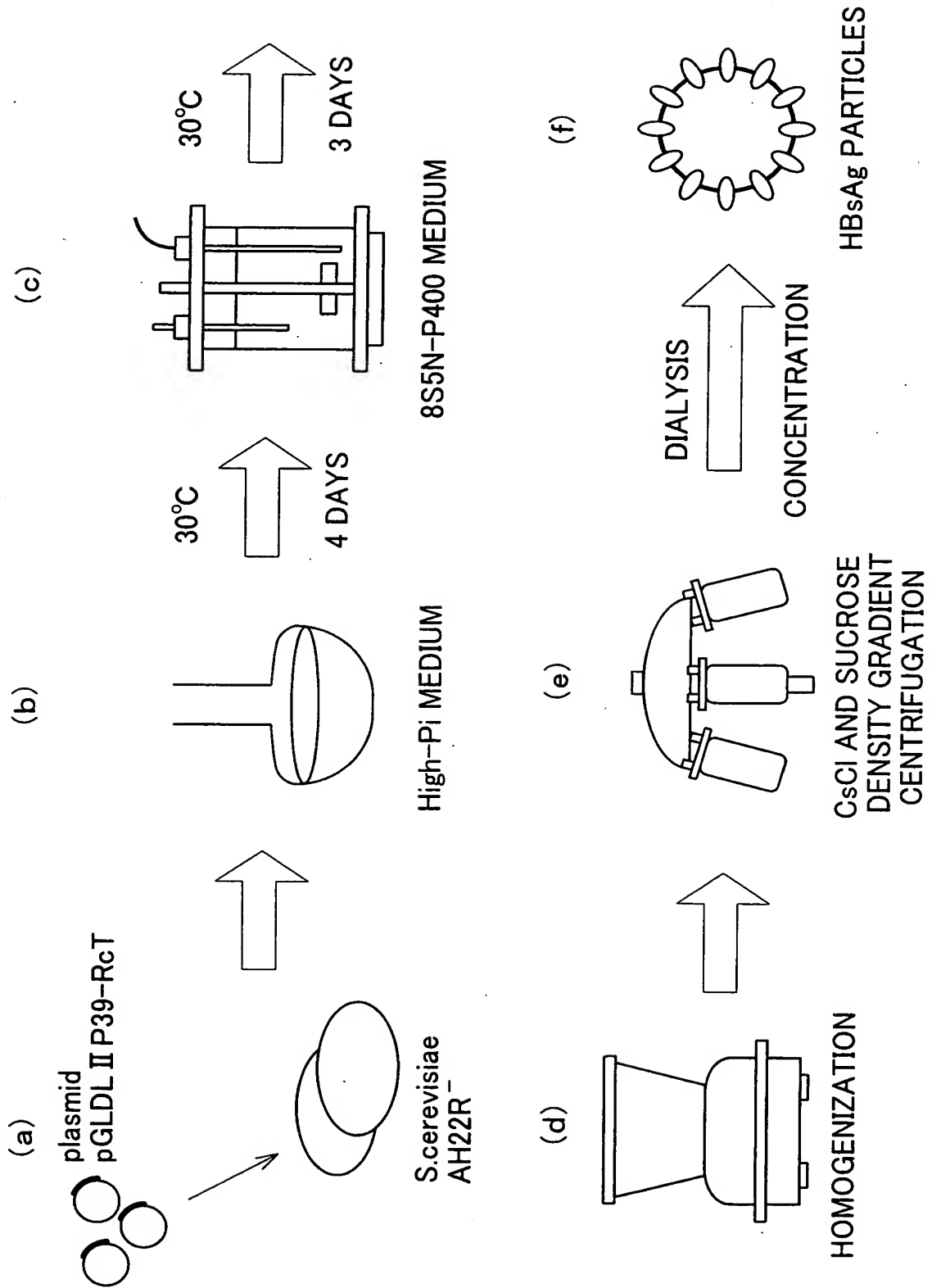
FIG. 1



- 1 PARTICLE FORMATION SUPPRESSING SITE
- 2 DIRECT RECEPTOR SPECIFIC TO HUMAN HEPATOCYTE
- 3 SUGAR CHAIN 1
- 4 INDIRECT RECEPTOR SPECIFIC TO HUMAN HEPATOCYTE  
(POLYMERIZED HUMAN SERUM ALBUMIN RECEPTOR)
- 5 TRANSMEMBRANE REGION 1
- 6 TRANSMEMBRANE REGION 2
- 7 SUGAR CHAIN 2
- 8 TRANSMEMBRANE REGION 3

2/8

FIG. 2



3/8

FIG. 3

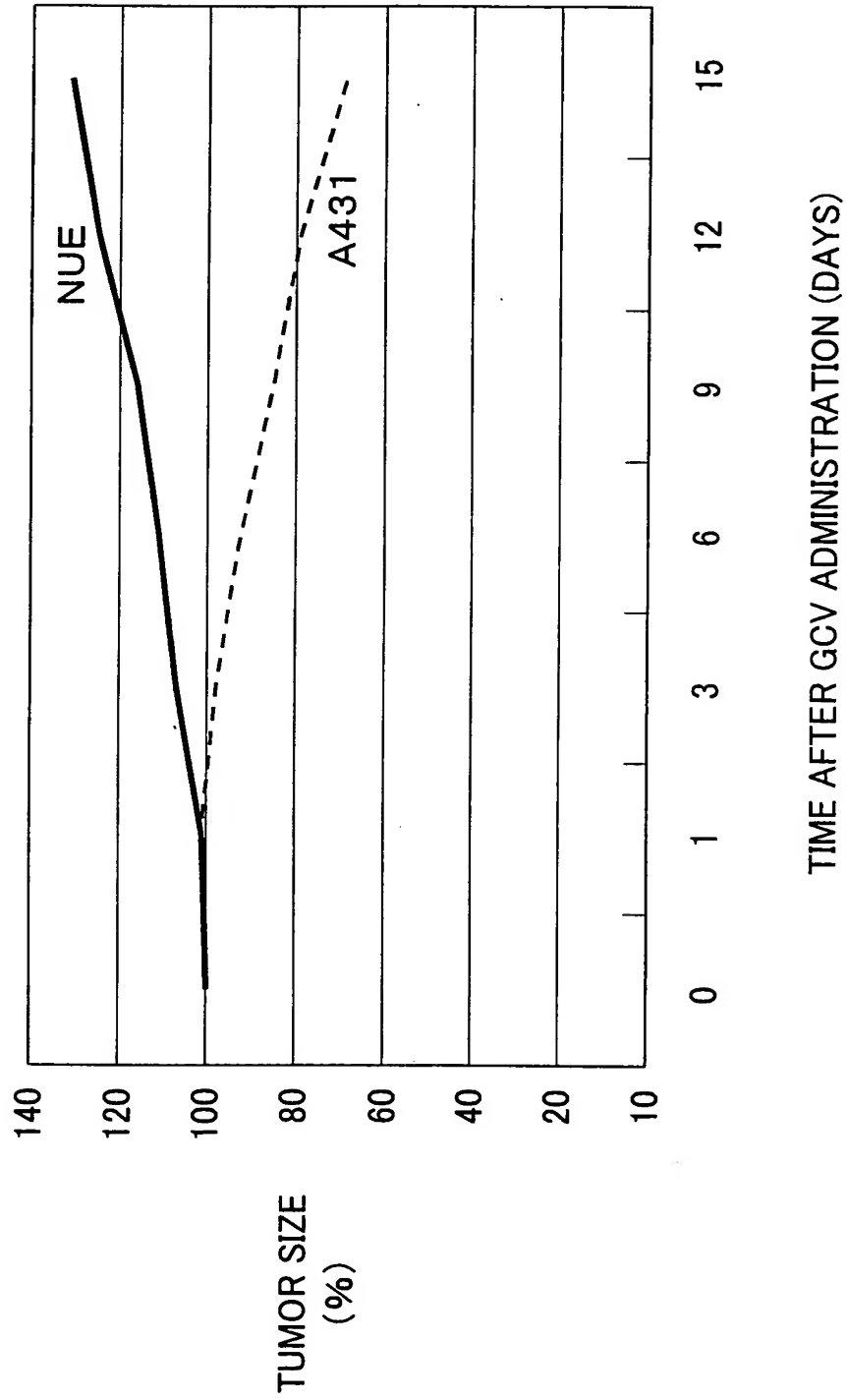


FIG. 4

|   |  |
|---|--|
| PROTEIN ATTACKING<br>CYTOPLASMIC RNA SUCH<br>AS RNase | Pancreatic type Rnases from vertebrates  |
|   | RNase 1 or Bovine RNase A  |
|   | Eosinophil derived neurotoxin  |
|   | Eosinophil cationic protein  |
|   | Liver RNase (RNase 4)  |
|   | Angiogenin   |
|   | Bovine seminal RNase   |
|   | Frog Rnases (Onconase etc.)  |
| PROTEIN OBSTRUCTING<br>TRANSMEMBRANE                  | Streptolysin(Streptococcus pyogenes)   |
|   | Cholesterol binding toxins (Streptococcus.<br>Bacillus. Clostridium. Listeria) |
|   | alpha-Toxin (Staphylococcus aureus)  |
|   | Delta-Toxin (Staphylococcus aureus) and<br>melittin (Apis mellifera)           |
|   | Aerolysin (Aeromonas hydrophila)   |
|   | Escherichia coli hemolysin   |
|   |  |
| PROTEIN OBSTRUCTING<br>SIGNAL TRANSDUCTION            | Cholera toxin (Vibrio cholerae)  |
|   | Heat-labile enterotoxins (Escherichia ColiD)                                   |
|   | Pertussis toxin (Bordetella pertussis)   |
|   | Exoenzyme C3 (Clostridium botulinum)   |
|   | Adenylate cyclase toxin (Bordetella sp.)                                       |
|   | Anthrax edema factor (Bacillus anthracis)                                      |
| PROTEIN OBSTRUCTING<br>PROTEIN SYNTHESIS              | Diphtheria toxin (Corynebacterium diphtheriae)                                 |
|   | Pseudomonas aeruginosa exotoxin A  |
|   | Shiga toxins (Shigella dysenteriae serotype I,<br>Escherichia Coli)            |
|   | Ricin (Ricinus communis)   |
|   | Ribosome-inactivating proteins   |
|   | alpha-Sarcin and related toxins (Aspergillus)                                  |
| PROTEIN DISTURBING<br>CYTOSKELETON                    | C2 toxin (Clostridium botulinum type C and D)                                  |
|   | Cytotoxic necrotizing factors (Escherichia coli)                               |
|   | Enterotoxin A and cytotoxin B (Clostridium<br>difficile)                       |
|   | ActA (Listeria monocytogenes)  |
|   | IcsA (Shigella flexneri)   |
|   | Zonula occludens toxin (Vibrio cholerae)                                       |

FIG. 5

|   |  |
|---|--|
| PROTEIN SUPPRESSING IMMUNITY OR INFLAMMATORY REACTION | Pyrogenic exotoxins (superantigens) (Staphylococcus aureus and Streptococcus pyogenes)                             |
|   | Anthrax lethal toxin (Bacillus anthracis)  |
|   | Leukocidins and gamma lysins (Staphylococcus sp.)  |
| PROTEIN DISTURBING MEMBRANE TRANSPORT                 | Tetanus neurotoxin (Clostridium tetani)  |
|   | VAMP-specific botulinum neurotoxins  |
|   | Botulinum neurotoxins type A and E (Clostridium botulinum)   |
|   | Botulinum neurotoxin type C (Clostridium botulinum)  |
|   | Vacuolating cytotoxin (Helicobacter pylori)  |
| PROTEIN DISTURBING SODIUM CHANNEL                     | alpha-Scorpion toxins  |
|   | beta-Scorpion toxins   |
|   | Excitatory insect selective neurotoxins from scorpion venoms   |
|   | Depressant insect selective neurotoxins from scorpion venoms   |
|   | mu-Conotoxins (Conus geographus)   |
|   | mu-Agatoxins (Agelenopsis aperta)  |
|   | Anthopleurin-A, -B, and -C (anemone toxin)   |
|   | Anemone toxins (type II)   |
|   | Calitoxins   |
| PROTEIN DISTURBING POTASSIUM CHANNEL                  | Kaliotoxin   |
|   | Scyllatoxin (Leiurus quinquestriatus hebraeus)   |
|   | Apamin (honey bee Apis mellifera)  |
|   | MCD peptide (honey bee Apis mellifera)   |
|   | Charybdotoxin and iberiotoxin (Leiurus quinquestriatus var. hebraeus and Buthus tamulus)                           |
|   | Margatoxin, noxiustoxin, and kaliotoxin (Centruroides margaritatus, Centruroides noxius, Androctonus mauretanicus) |
|   | Dendrotoxins (Dendroaspis species)   |
|   | Sea anemone potassium channel toxins   |

FIG. 6

|   |  |
|---|--|
| PROTEIN DISTURBING<br>CALCIUM CHANNEL                           | Omega-Conotoxins ( <i>Conus</i> spp.)  |
|   | Omega-Agatoxins ( <i>Agelenopsis aperta</i> )  |
|   | Omega-Grammotoxin SIA ( <i>Grammostola spatulata</i> Chilean pink tarantula)           |
|   | Hololena toxin ( <i>Hololena curta</i> )   |
|   | PLTXII ( <i>Plectreurys tristes</i> )  |
|   | Calciseptine ( <i>Dendroaspis polylepis</i> )  |
|   | Calcicludeine ( <i>Dendroaspis angusticeps</i> )                                       |
|   | beta-Leptinotarsin-h   |
|   | Taicatoxin ( <i>Oxyuranus scutellatus scutellatus</i> )                                |
|   |  |
| PROTEIN DISTURBING<br>ACETYLCHOLINE<br>RECEPTOR                 | alpha-Bungarotoxin ( <i>Bungarus multicinctus</i> )                                    |
|   | alpha-Cobratoxin ( <i>Naja kaouthia</i> )  |
|   | Erabutoxins ( <i>Laticauda semifasciata</i> )  |
|   | Toxin alpha (' <i>Naja nigricollis</i> ')  |
|   | kappa-Bungarotoxin ( <i>Bungarus multicinctus</i> )                                    |
|   | alpha-Conotoxins ( <i>Conus</i> spp.)  |
|   | Snake toxins against muscarinic acetylcholine receptors                                |
|   | Muscarinic toxin-1~5, -7, m1-toxin from green mamba ( <i>Dendroaspis angusticeps</i> ) |
|   | Muscarinic toxin-alpha, -beta from black mamba ( <i>Dendroaspis polylepis</i> )        |
| PROTEIN DISTURBING<br>RYANODINE RECEPTOR<br>CALCIUM ION CHANNEL | Helothermine ( <i>Heloderma horridum horridum</i> )                                    |

FIG. 7

|   |  |
|---|--|
| PROTEIN DISTURBING<br>PRE-SYNAPSE               | beta-Bungarotoxin ( <i>Bungarus multicinctus</i> )                       |
|   | Rattlesnake venom neurotoxins: crotoxin-related proteins                 |
|   | Ammodytotoxins ( <i>Vipera ammodytes ammodytes</i> )                     |
|   | Notexins ( <i>Notechis scutatus scutatus</i> )                           |
|   | Textilotoxin ( <i>Pseudonaja textilis textilis</i> )                     |
|   | Tai poxin  |
|   | alpha-Latrotoxin (black widow spider)                                    |
|   | alpha-Latroinsectotoxin ( <i>Latrodectus mactans tred ecimguttatus</i> ) |
|   | Pardaxin ( <i>Pardachirus marmoratus</i> )                               |
|   | Palytoxin (Corals of the spp. <i>Palythoa</i> )                          |
|   | Equinatoxins ( <i>Actinia equina</i> L., sea anemone)                    |
| PROTEIN DISTURBING<br>GLUTAMIC ACID<br>RECEPTOR | Conantokins ( <i>Conus</i> spp.)   |

MS 432 8 S 10/10/04 10:10

8/8

FIG. 8

|                   |         | TIME AFTER GCV ADMINISTRATION<br>(DAYS) |     |     |     |     |     |     |
|-------------------|---------|---|-----|-----|-----|-----|-----|-----|
|                   |         | 0                                       | 1   | 3   | 6   | 9   | 1 2 | 1 5 |
| TUMOR SIZE<br>(%) | A 4 3 1 | 100                                     | 101 | 98  | 92  | 85  | 79  | 69  |
|                   | NUE     | 100                                     | 101 | 106 | 111 | 116 | 125 | 131 |